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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/673,352	09/30/2003	Lee Johnson	NC 84,495	8469

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EXAMINER	
BOWERS, NATHAN ANDREW	

ART UNIT	PAPER NUMBER
1797	

MAIL DATE	DELIVERY MODE
04/10/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/673,352	JOHNSON ET AL.	
	Examiner	Art Unit	
	NATHAN A. BOWERS	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 25 January 2008 has been entered.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1) Claims 28-32, 35, 39 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Xu (US 20050112544) in view of Hoff (US 20050054969).

With respect to claims 28, 39 and 40, Xu discloses an electroporation device comprising a microelectrode plate (Figure 3) constructed from conducting electrode material. Figure 4B indicates that a plurality of electrodes are arranged on a surface of the plate, such that the electrodes are adapted to support a monolayer of cells and/or lipid vesicles. Each of the electrodes are independently addressable and are independently conductive therethrough. This is taught in paragraphs [0041]-[0044], [0192] and [0198]. Xu teaches that biological materials supported on the electrodes are porated when appropriate voltage pulses are applied to the electrodes. Xu describes that the electroporation device is fabricated such that it is positioned within a common laboratory fluid chamber, such as a microtiter plate. The microelectrode plate forms the bottom surface of the fluid chamber, and the microtiter plate forms the top and sidewall portions. This is disclosed in paragraph [0201]. Xu, however, does not clearly indicate that the microelectrode plate is in communication with an electronic array containing a plurality of circuits forming a 2D array of unit cells.

Hoff discloses a device for the electroporation of cultured cells. A stimulator array is formed by electrodes (Figure 1:14 and Figure 1:15) that are capable of applying spatially variant voltages for electroporation. Paragraph [0020] states that the stimulator array comprises at least one anode and at least one cathode, and is structured for connection with a voltage source. This is additionally described in paragraphs [0018]-[0021], [0036]-[0038] and [0043]. Hoff specifically teaches that the electrode materials form anodes and cathodes that cause electroporation when a voltage is applied. In Figure 5, Hoff discloses a particular embodiment in which an electronic array (160) containing an array of unit cells is positioned underneath and is in communication with conducting electrode material (170) arranged to interact with cells.

Xu and Hoff are analogous art because they are from the same field of endeavor regarding electroporation devices.

At the time of the invention, it would have been obvious to ensure that the apparatus of Xu is constructed so that an electronic array of unit cells is positioned below the disclosed microelectrode plate. Hoff teaches that this arrangement is beneficial because it allows one to construct a high-density electrode array capable of interacting with a substantial number of cells simultaneously. Xu already teaches that it is known to apply a time varying voltage of independent electrode clusters to induce electroporation. It would have been obvious to utilize an electronic array to accomplish this task because circuit materials are inexpensive, easily machined, and capable of facilitating high densities of implanted electrodes.

With respect to claim 29, Xu and Hoff disclose the apparatus set forth in claim 28 as set forth in the 35 U.S.C. 103 rejection above. Xu and Hoff each additionally describe the use of

anodes and cathodes to apply an electroporation voltage to cells in communication with the electrodes.

With respect to claims 30-32, Xu and Hoff disclose the apparatus set forth in claim 30 as set forth in the 35 U.S.C. 103 rejection above. Furthermore, Xu teaches that the electrodes can be arranged in essentially any configuration. Specifically, Xu indicates in Figure 4B that electrodes are arranged in pairs. Figures 4 and 7F are examples of a "center surround" geometry, and Figure 7C discloses a parallel column arrangement. Each of these arrangements are repeated in an array across the microelectrode plate.

In addition, Hoff indicates in Figures 1 and 5 that a plurality of anodes and cathodes are arranged in alternating fashion. Each cathode is surrounded by many of anodes. Generally, the duplication and rearrangement of parts is not sufficient to overcome the prior art. See MPEP 2144.04. In this case, varying the number and positioning of the anodes and cathodes is not considered to be a patentable difference.

With respect to claim 35, Xu and Hoff disclose the apparatus set forth in claim 30 as set forth in the 35 U.S.C. 103 rejection above. The microtiter plates disclosed by Xu are commonly made from clear polymer or glass materials.

2) Claims 33 and 34 rejected under 35 U.S.C. 103(a) as being unpatentable over Xu (US 20050112544) in view of Hoff (US 20050054969) as applied to claim 28, and further in view of Merritt (US 20040241965).

Xu and Hoff disclose the apparatus set forth in claim 28 as set forth in the 35 U.S.C. 103 rejection above, however do not expressly disclose that the electrode material comprises glass hybridized to the simulator array with indium bumps.

Merritt discloses a high aspect ratio microelectrode array useful in the delivery and detection of electrical signals at discrete, spatially resolved locations. Paragraph [0037] indicates that it is known in the art to utilize indium bumps to make electrical connections between two arrays of electrical contacts.

Xu, Hoff and Merritt are analogous art because they are from the same field of endeavor regarding electrical manipulation devices.

At the time of the invention, it would have been obvious to connect the microwire glass electrodes to the simulator array using the well known process of indium bump bonding. Merritt teaches in paragraph [0037] that wire electrodes easily can be pushed into indium in order to create an electrical connection between an array of electronic unit cells and an array of microelectrodes.

3) Claims 36-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Xu (US 20050112544) in view of Hoff (US 20050054969) as applied to claim 28, and further in view of Dzekunov (US 20040197883).

Xu and Hoff disclose the apparatus set forth in claim 28 as set forth in the 35 U.S.C. 103 rejection above, however the fluid chambers disclosed by Xu do not include inlet and outlets in communication with a pump and valves.

Dzekunov discloses an electroporation device that comprises a fluid flow chamber through which cell samples are allowed to move. The chamber comprises electrodes that apply voltages sufficient to porate the cells as they flow through the chamber. The chamber includes inflow and outflow ports, valves, tubing, and a pump. This is described in Figure 12 and paragraphs [0191]-[0193] and [0240]-[0242].

Xu, Hoff and Dzekunov are analogous art because they are from the same field of endeavor regarding electroporation apparatuses.

At the time of the invention, it would have been obvious to ensure that the electroporation system proposed by Xu is provided with a fluid flow chamber that comprises access ports, valves, and a pump. More specifically, it would have been apparent to form a flow cell chamber around the stimulator array and the conduction portion in order to form a reaction chamber within which cells and tissues can undergo electroporation. Dzekunov teaches that flow cells are beneficial because they can be used to automatically porate and treat a large number of cells in a short amount of time. The use of an automatic flow cell system is desirable because it can be easily and inexpensively operated when compared to other electroporation systems.

Response to Arguments

Applicant's arguments filed 25 January 2008 with respect to the 35 U.S.C. 102 rejections involving Hoff have been fully considered and are persuasive. These rejections have been withdrawn.

Applicant's arguments filed 25 January 2008 with respect to the 35 U.S.C. 103 rejections involving Hoff and Dzekunov have been fully considered and are persuasive. Therefore, these rejections have been withdrawn. However, upon further consideration, a new ground of rejection is made in view of the combination of Xu and Hoff.

Xu does not suffer from the same deficiencies as Hoff because Xu clearly discloses that a fluid is arranged on one side of the conducting electrode material. The fluid chamber forms a top and at least one sidewall capable of retaining fluid during electroporation.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NATHAN A. BOWERS whose telephone number is (571)272-8613. The examiner can normally be reached on Monday-Friday 7 AM to 4 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gladys Corcoran can be reached on (571) 272-1214. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/William H. Beisner/
Primary Examiner, Art Unit 1797

/Nathan A Bowers/
Examiner, Art Unit 1797